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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/320,100	05/26/1999	DEBORAH ANN ANSALDI	P1363R1	4114

7590 11/18/2002

ATTN JANET E HASAK
GENENTECH INC
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER

HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 11/18/2002

25

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/320,100

Applicant(s)

ANSALDI ET AL.

Examiner

Anne Holleran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Prosecution is hereby reopened and the finality of the previous Office action is withdrawn.

2. The amendment filed July 30, 2002 is acknowledged. Claim 1 has been amended and claims 14 and 15 added.

Claims 1-15 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The declaration of Dr. Stephen Cramer, filed under 37 C.F.R. 1.132, has been considered.

Claim Rejections Withdrawn:

4. The rejections of claims 1-13 under 35 U.S.C. 102(b), 102(a), and 103(a) are withdrawn upon further consideration and in view of the amendment.

New Claim Rejections:

5. Claims 1-3 and 5-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for separating monomers from a mixture of monomers, dimers and multimers of BSA or anti-IGE, does not reasonably provide enablement

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for methods for separating monomers from a mixture of monomers, dimers or multimers of any protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See *Ex parte Forman*, 230 USPQ 546, BPAI, 1986.

Claims 1-3 and 5-15 are broadly drawn to methods for the separation of monomers from a mixture of monomers, dimers or multimers of any protein, the method consisting essentially of applying the mixture to an ion exchange chromatography resin, wherein if the ion exchange resin is a cation exchange resin then the pH of the mixture is between 4-7, and wherein if the ion exchange resin is an anion exchange resin then the pH of the mixture is between 6-9.

The specification provides examples of the method for the separation of monomers of BSA from dimers and multimers of BSA, and for the separation of monomers of anti-IGE from dimers and multimers of anti-IGE. The specification teaches that pH the equilibration buffer of the mixture of monomers, dimers and multimers should be in the range of 4-9, and teaches the specific pH values of the buffers for the specific examples. However, the specification fails to teach the rationale for choosing the specific pH values of the buffers used in the separations shown in the examples.

The pH of the equilibration buffer appears to be an essential feature of the claimed methods. For example, Arndt (Biochemistry, 1998, 37: 12918-12926) teaches that pH is a factor in the conversion of scFv monomers to dimers.

The prior art provides no guidance in the selection of pH for mixtures of monomers, dimers and multimers, and whether pH is a factor that must be controlled in the selection of ion exchange conditions for a method of separating monomers from dimers and multimers.

The prior art also provides an example of the claimed method where ion exchange chromatography was used for purification of scFv monomers, dimers and multimers (see Yang, Molecular Immunology (1995) 32(12): 873-881; page 876-877, bridging paragraph) where the method was unsuccessful. Yang applied solubilized inclusion bodies (a mixture consisting essentially of monomers, dimers and multimers of the scFv) to a Mono-S column, but failed to separate the monomers from the dimers and multimers.

Therefore, in view of the lack of teachings in the specification for how to choose the appropriate pH of the equilibration buffer, and further in view of the lack of guidance in the prior art, the specification fails to enable the full scope of the claimed methods, where the methods are used to separate the monomers from the dimers or multimers of any protein. To practice the full scope of the invention one would have to engage in undue experimentation to discover the appropriate pH for the equilibration buffer, because the specification lacks a teaching of the rationale for choosing the pH of the buffer containing the proteins of the exemplified embodiments.

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6. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it lacks a recitation of an active step for recovering the monomer.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892.


Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

ALH

Anne L. Holleran
Patent Examiner
November 8, 2002


ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600